Complete Summary

GUIDELINE TITLE

Major depression in adults for mental health care.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Major depression in adults for mental health care. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 May. 52 p. [154 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Major depression (single and recurrent major depressive disorders)

This guideline does not necessarily pertain to depression within the context of bipolar disorders, adjustment disorders, medical conditions, or others.

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To increase the use of Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision (DSM-IV TR) criteria in the detection and diagnosis of major depression
- To improve the efficacy of the treatment through diagnosis of major depression
- To improve the outcomes of treatment for major depression
- To improve the adherence and maintenance of appropriate treatments for patients diagnosed with major depression by having follow-up contacts with a health care professional
- To improve communication between the primary care physician and the mental health care provider (if patient is comanaged)

TARGET POPULATION

Adults greater than 18 years of age with major depressive episodes in an outpatient setting of mental health care providers

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Multi-axial assessment, including use of the Global Assessment of Functioning (GAF) scale
2. Assessment of depression using Diagnostic and Statistical Manual of Mental Disorders, 4th edition Text Revision (DSM-IV TR) criteria
3. Evaluation for other mood and anxiety disorders or somatoform disorders
4. Assessment of need for hospitalization and suicidal tendencies
5. Substance abuse/dependency assessment, using the CAGE-AID (AID = Alcohol Illicit Drugs) screen

Treatment

1. Patient education

2. Pharmacotherapy
    - Antidepressants
        - Selective serotonin reuptake inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)
        - Serotonin-norepinephrine reuptake inhibitors (e.g., venlafaxine, venlafaxine extended release)
        - Dopamine-norepinephrine reuptake inhibitors (e.g., bupropion, bupropion sustained release)
        - Norepinephrine-serotonin modulator (e.g., mirtazapine)
        - Tricyclic and tetracyclic antidepressants
            - Tertiary amine tricyclics (e.g., amitriptyline, clomipramine, doxepin, imipramine, trimipramine)
            - Secondary amine tricyclics (e.g., desipramine, nortriptyline, protriptyline)
            - Tetracyclics (e.g., amoxapine, maprotiline)
        - Serotonin modulators (e.g., nefazodone - black box warning, trazodone - for sleep primarily)
        - Monoamine oxidase inhibitors (MAOIs)
            - Irreversible, nonselective (e.g., phenelzine, tranylcypromine)
            - Reversible MAOI-A (e.g., moclobemide)
        - Selective noradrenaline reuptake inhibitor (e.g., reboxetine)

3. Electroconvulsive therapy (ECT)
4. Light therapy
5. Other strategies: augmentation therapy (including combination of different classes of antidepressants, combination of lithium with antidepressants, and combination of antidepressants with triiodothyronine, carbamazepine/valproic acid, or risperidone); switch therapy; psychotherapy (specifically, cognitive-behavioral therapy, interpersonal therapy, problem-solving therapy, and brief psychodynamic supportive therapy); exercise; herbals and dietary supplements (Note: Hypericum perforatum [St. John's wort], other herbal remedies and dietary supplements such as kava-kava, Omega-3 fatty acid, and valerian root were considered but not recommended); and hospitalization; (Note: vagus nerve stimulation, transcranial magnetic stimulation, and acupuncture were considered but not recommended)
6. Continuation and maintenance treatment for 6 to 12 months

MAJOR OUTCOMES CONSIDERED

- Risk factors for depression, anxiety, and panic disorder
- Risk for and rate of suicide or suicide attempts

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

No additional description of literature search strategies is available.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of "Critical Review".

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group: Second Draft

Following the completion of the "Critical Review" period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary, and a written response is prepared to address each of the suggestions received from medical groups. Two members of the Committee on Evidence-Based Medicine carefully review the Critical Review input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of two questions: (1) Have the concerns of the medical groups been adequately addressed? (2) Are the medical groups willing and able to implement the guideline? The committee then either approves the guideline for pilot testing as submitted or negotiates changes with the work group representative present at the meeting.

Pilot Test

Medical groups introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three months. Comments and suggestions are solicited in the same manner as used during the "Critical Review" phase.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Committee on Evidence-Based Medicine reviews the revised guideline and approves it for implementation.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations are presented in the form of an algorithm with 14 components, accompanied by detailed annotations. The algorithm is provided for Major Depression In Adults For Mental Health Care. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) definitions are provided at the end of the "Major Recommendations" field.

Clinical Highlights

1. A reasonable way to evaluate whether a system is successfully functioning in its diagnosis, treatment plan, and follow-up of major depression is to consider:
    - How well the diagnosis is documented
    - How well the treatment team engages and educates patients/families
    - How well the ongoing patient contacts are documented
    - How well the outcomes are measured and documented

    (Introduction -see the original guideline document)

2. Presentations for depression include:
    - Multiple somatic complaints, weight gain/loss, mild dementia
    - Multiple (>5/year) medical visits; more than one organ system, with the absence of physical findings
    - Fatigue
    - Work or relationship dysfunction/changes in interpersonal relationships
    - Sleep disturbances

    (Annotation #1)

3. Evaluate depressed patients using all five axes in the Diagnostic and Statistical Manual for Mental Disorders, 4th Edition Text Revision (DSM-IV TR) criteria and provide documentation for this evaluation.
    - Axis I: Clinical Disorders, other conditions that may be a focus of clinical attention
    - Axis II: Personality Disorders, borderline intellectual functioning, or mental retardation
    - Axis III: General Medical Conditions
    - Axis IV: Psychosocial and Environmental Problems
    - Axis V: Global Assessment of Functioning

    (Annotation #2)

4. Assess patients who present with safety risks to themselves or others, are unable to care for themselves, or experience psychotic thinking. Those patients should be considered for emergency treatment/hospitalization. (Annotation #5)
5. It is important that treatment involve agreement between the patient and his or her provider involved in managing this condition. Treatment of a major depressive episode may involve initiation of pharmacotherapy. Current data does not support the efficacy of one antidepressant or family of antidepressants over another. (Annotation #11)
6. Acute treatment (usually the first 3 months of treatment) refers to treating with antidepressant medication in order to achieve remission of depressive symptoms. Remission is defined as having minimal residual symptoms (Hamilton Depression Scale score less than 7 or Patient Health Questionnaire [PHQ-9] score of 4 or less.) Continuation therapy is the phase where one continues to treat with antidepressants in order to keep the patient free of symptoms for the duration of the current episode. (Annotation #14)
7. If there is less than a 25% reduction in symptoms when evaluated at 4 to 6 weeks, switch to a different medication. If there is a partial response and side effects are not prohibitive, increase the dose. If the patient has not achieved

remission when reevaluated after an additional 4 to 6 weeks of a treatment regimen, other strategies should be considered. (Annotation #15)

Major Depression In Adults For Mental Health Care Algorithm Annotations

1. Evaluate Psychiatric Symptoms and Comorbidities

   Clinicians should consider the diagnosis of depression not only when patients present with one of the nine symptoms of a major depressive episode, but also when they present with unexplained somatic symptoms, irritability, anxiety, frequent unnecessary visits to physicians, headaches, and other symptoms.

   ### Multiaxial Assessment

   This system involves an assessment on each of five axes. Each axis refers to a different domain of information that may help the clinician assess the patient, plan treatment, and predict outcome.

   #### Axis I: Clinical disorders, other conditions that may be a focus of clinical attention

   This axis is for listing all diagnoses of mental illness and psychiatric conditions, except for the personality disorders and mental retardation.

   #### Axis II: Personality disorders, borderline intellectual functioning, or mental retardation

   This axis is for reporting personality disorders, mental retardation, developmental learning disorders, and prominent maladaptive personality features and defense mechanisms.

   #### Axis III: General medical conditions

   If mood disorder is due to a general medical condition, then it is out of the guideline.

   Current general medical conditions which are or may be potentially relevant to the listed Axes I and II disorders are reported in this axis.

   There are no definitive studies which support recommendations for or against routine laboratory or medical screening.

   #### Axis IV: Psychosocial and environmental problems

   Psychosocial and environmental problems which may affect the diagnosis, treatment, and prognosis of Axes I and II are noted here.

   When using the "Multiaxial Evaluation Report Form," the clinician should identify the relevant categories of psychosocial and environmental problems

and indicate the specific factors involved. If a recording form with a checklist of problem categories is not used, the clinician may simply list the specific problems on Axis IV.

Categories of problems to be considered include:

- Problems with primary support group
- Problems related to the social environment
- Educational problems
- Occupational problems
- Housing problems
- Economic problems
- Problems with access to health care services
- Problems related to interaction with the legal system/crime
- Other psychosocial and environmental problems

Axis V: Global assessment of functioning

Axis V is for reporting the clinician's judgment of the individual's overall level of functioning. This information is useful in rating severity, planning treatment, and measuring its impact, as well as in predicting outcome.

See Appendix A in the original guideline document for the "Global Assessment of Functioning Scale."

Evidence supporting this recommendation is of classes: C, R

2. Does Patient Fit DSM-IV TR Criteria for Major Depressive Episode?

DSM-IV TR criteria for major depressive episode:

A. Five or more of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-congruent delusions or hallucinations.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
3. Significant weight loss when not dieting or weight gain (e.g., change of more than 5% of body weight in a month) or decrease or increase in appetite nearly every day
4. Insomnia or hypersomnia nearly every day

5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a mixed episode.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct physiological effects of a substance (e.g., abuse of a drug, a medication) or a general medical condition (e.g., hypothyroidism).
E. The symptoms are not better accounted for by bereavement (i.e., after the loss of a loved one); the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

The assessment of major depressive disorders should include the DSM-IV TR numerical rating of the disorder with all 5 digits, thus including a severity rating. For example, 296.22 [Major depressive disorder, single episode, moderate severity].

3. Consider Other Mood and Anxiety Disorders or Somatoform Disorders/Out of Guideline

Patients with some depressive disorders who do not meet full DSM-IV TR criteria for major depression often respond positively to antidepressant medication and/or psychotherapy. Emerging evidence also supports the use of bright light therapy in some of the cases of milder depression.

Presentations particularly suggestive of an anxiety disorder include:

- Medically unexplained symptoms of autonomic excitation such as:
  - cardiac (chest pain, atypical chest pain, hyperventilation, palpitations, shortness of breath)
  - gastrointestinal (epigastric distress, irritable bowel syndrome)
  - neurologic (headache, dizziness, paresthesias)
  - panic attacks
- Emergency room visit for medically unexplained somatic symptoms, particularly chest pain

These symptoms can cause significant impairment, suffering, and disability. Antidepressants should be considered, though the evidence for their efficacy

is less well established with these disorders than with major depression. Other depression categories include Dysthymic Disorder and Depressive Disorder NOS (not otherwise specified).

Evidence supporting this recommendation is of classes: A, M

4. Is Patient Unsafe to Self or Others?

Many factors go into the decision to hospitalize a depressed patient. Some of the most salient include:

- Suicidal thoughts and/or plans which make the clinician uncertain of the patient's safety
- Assaultive or homicidal thoughts and/or plans which make the clinician uncertain about the safety of the patient or others
- Inability to care for the self/family
- Psychotic thinking

Assessment of Suicidal Tendencies

There are no good predictors of suicide. History which the clinician should consider includes, but is not limited to:

- Panic attacks and/or severe psychic anxiety
- Depressed mood
- Recent loss by death, divorce, or separation
- Substance abuse
- Severe hopelessness, or helplessness
- Insomnia
- Severe anhedonia
- Personality disorder and/or physical illness
- Previous history of suicide attempts
- Frequent suicidal ideation
- Concrete suicide plan
- Family history of suicide
- Single status
- Diminished concentration
- Elderly Caucasian and Asian men over the age of 65 years and Asian women over 80 years are at disproportionate risk

While it is important to inquire about suicidal tendencies and to account for risk factors, research has shown that all attempts to predict suicidal behavior are somewhat unreliable. Nonetheless, the clinician should routinely address concerns about suicide and document this assessment. The presence of one or more of the factors cited above does not, in and of itself, justify hospitalization or emergency treatment. Clinical judgment as to the likelihood of imminent harm to the patient or others is the most important consideration.

Evidence supporting this recommendation is of classes: D, R

6. Is Active Substance Abuse/Dependency Present?

The CAGE(AID) Screen

Current alcohol or other drug problems can be screened by asking a few questions that can be easily integrated into a clinical interview. A common screen is the CAGE screen.

The CAGE or CAGE(AID) should be preceded by two questions:

1. Do you drink alcohol?
2. Have you experimented with drugs?

If the patient has experimented with drugs, ask the CAGE(AID) questions. CAGE(AID) questions are modified with italicized text.

CAGE(AID) Screen

Have you ever:

C felt you ought to *cut* down on your drinking (or drug use)?
A had people *annoy* you by criticizing your drinking (or drug use)?
G felt bad or *guilty* about your drinking (or drug use)
E had a drink (or drug use) as an *eye opener* first thing in the morning to steady your nerves or get rid of a hangover or to get the day started?

If substance abuse is present or suspected, consider referral for substance abuse assessment.

Each affirmative response earns one point. One point indicates a possible problem. Two points indicate a probable problem.

Evidence supporting this recommendation is of classes: C, R

7. Evaluate and Treat for Substance Abuse

The medical literature does not support definitive statements about the best way(s) to treat patients who are diagnosed with both major depression and substance abuse/dependence. The majority of studies reviewed indicate that success in treating abuse/dependence on alcohol, cocaine, and other abused substances is more likely if accompanying depression is addressed. Fewer investigators have looked at whether treating substance abuse is helpful in reducing major depression. There is some evidence that patients with major depression that is secondary to their substance abuse may have remission of their depressed mood once the substance abuse is treated. However, it is difficult to separate secondary depression from primary depression that predates or is separate from the substance use.

Studies to assess the efficacy of concurrent treatment of major depression and substance abuse are limited in number and of variable quality. Although results are not fully consistent, the preponderance of available evidence

suggests that pharmacotherapy can be of benefit in treating both chemical abuse and depression in patients who have both disorders. Agents studied include amantadine (a dopamine agonist), desipramine (a tricyclic antidepressant), and fluoxetine (a selective serotonin reuptake inhibitor [SSRI]).

The algorithm reflects the uncertainty in this area. At box #6 (refer to the original guideline document) it splits into two possible paths. If yes – a depressed patient is felt to have substance abuse issues, treatment of the substance abuse should be considered, either before or while treating the depression. However, if no – a depressed patient refuses substance abuse treatment, or has failed it several times, it is appropriate to focus primarily on the depression. It is reasonable to attempt to treat the depression while continuing to assist the patient to work toward efforts to decrease or eliminate their substance abuse. Continue to ask about addiction issues and to emphasize the need for sobriety. If the patient continues to have depressive symptoms despite antidepressant therapy, this could be pointed out to the patient as one more reason to seek treatment for substance abuse.

Evaluation and treatment for chemical dependency is beyond the scope of this guideline. A referral may be appropriate.

Evidence supporting this recommendation is of classes: A, C

9. Reevaluate and Treat for Primary or Secondary Condition

Be aware of comorbidities. Relapse rates may be much higher unless the primary medical illness is simultaneously treated.

Be aware of ongoing mental illness diagnosis or other mental health illnesses and comorbidities.

Some patients presenting with a major depressive episode have a bipolar disorder, for which effective treatment may differ significantly from other depressed patients. When assessing a patient, consider asking about manic or hypomanic episodes.

Has there been a distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week? During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep
3. More talkative than usual or pressure to keep talking
4. Flight of ideas or subjective experience that thoughts are racing
5. Distractibility
6. Increase in goal-directed activity or psychomotor agitation
7. Excessive involvement in pleasurable activities that have a high potential for painful consequences

If these criteria are met, the patient may have a bipolar mood disorder. Treatment for this falls out of the scope of this guideline.

Ask patients with major depression about a history of manic symptoms (abnormally elevated, expansive, or irritable mood). Patients with a history of manic (bipolar) symptoms now presenting with major depression may develop manic symptoms with antidepressant drugs. If other psychiatric problems are present or suspected, involve appropriate professionals. If other psychiatric problems such as psychosis or eating disorders are suspected or present, involve the appropriate professionals.

10. Educate and Engage Patient / Institute Treatment Plan / Establish Follow-Up

Educate and Engage Patient

Depression is diagnosed on the basis of specific DSM-IV TR criteria obtained through a clinical interview.

Successful programs for the treatment of depression include:

- Organized treatment protocols
- Structured follow-up protocols
- Systematic monitoring of treatment adherence and effectiveness

Patient Education

1. Successful care of major depression as an illness requires active engagement of each patient and their family and on-going patient education, beginning at the time of diagnosis. It is important for the patient to consider and adopt some self-care responsibilities, which may range from simply demonstrating reliable behavior in taking medications and calling the provider with side effects to agreeing to participate in sessions, journaling and completing homework, which is necessary for some cognitive behavioral therapies. Written materials are helpful to reinforce information shared during the discussion. Patients who commit to some self-care responsibilities and receive this education compared with those who do not are more likely to continue, rather than prematurely abandon treatment, and are more likely to attain better outcomes. Education topics should include:
    - The cause, symptoms and natural history of major depression
    - Treatment options (trial and error approach)
    - Information on what to expect during the course of treatment
    - How to monitor symptoms and side effects
    - Follow-up protocol (office visits and/or telephone contacts)
    - Early warning signs of relapse or recurrence
    - Length of treatment

2. When antidepressant therapy is prescribed, the following key messages should be highlighted to support medication adherence and completion:

- Side effects from medication often precede therapeutic benefit and typically recede over time. It is important to expect some discomfort prior to benefit.
- Successful treatment often involves dosage adjustments and/or trial of a different medication at some point, to maximize response and minimize side effects.
- Most people need to be on medication at least 6 to 12 months after adequate response to symptoms.
- It usually takes from 2 to 6 weeks before improvement is seen.
- Take the medication as prescribed, even after one feels better.
- Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dosage schedule.

Evidence supporting this recommendation is of class: R

Exercise

Evidence suggests that physical activity might be a useful tool for easing major depression symptoms. Among individuals with major depression, exercise therapy is feasible and is associated with significant therapeutic benefit, especially if exercise is continued over time. When prescribing exercise as an adjunct to medication and psychotherapy, the complexity and the individual circumstances of each patient must be considered. When prescribing an exercise prescription, several caveats apply:

- Anticipate barriers – hopelessness and fatigue can make physical exertion difficult
- Keep expectations realistic – some patients are vulnerable to guilt and self-blame if they fail to carry out the regime
- Introduce a feasible plan – walking, alone or in a group, is often a good option
- Accentuate pleasurable aspects – the specific choice of exercise should be guided by the patient's preferences, and must be pleasurable
- State specifics – a goal of 30 minutes of moderate-intensity exercise, 3-5 days a week is reasonable for otherwise healthy adults
- Encourage adherence – greater antidepressant effects are seen when training continues beyond 16 weeks

Evidence supporting this recommendation is of classes: A, R

Institute Treatment Plan

Psychotherapy

- Outcome studies support the efficacy of several psychotherapeutic approaches (cognitive-behavioral, interpersonal, structured educational group therapy).
- If care originates in psychiatry, consider early referral for psychotherapy if psychological and psychosocial issues are prominent and/or patient requests it. Referral for psychotherapy may have maximum benefit as symptom severity diminishes.

- Supportive therapy by the physician in the primary care setting is not the same as a course of psychotherapy with a mental health professional. However, education, support and reassurance by the physician are critical. Support/reassurance includes asking the patient for his/her ideas regarding the cause of the depression and about their expectations of recovery. Inform patients with depression that they have a good chance of improving.

Evidence supporting this recommendation is of classes: A, D, R

Medications

For antidepressant medications, adherence to a therapeutic dose and meeting clinical goals are more important than the specific drug selected.

Health care providers should carefully evaluate patients in whom depression persistently worsens, or emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms, to determine what intervention, including discontinuing or modifying the current drug therapy, is indicated. The provider should instruct their patients, the patient's families and the patient's caregivers to be alert for the emergence of agitation, irritability, and the other symptoms described above, as well as the emergence of suicidality and worsening depression, and to report such symptoms immediately to the patient's health care provider.

Selection of an Antidepressant Medication

Antidepressant drug selection should be based on:

- the patient's history of response to previous antidepressant medications (if any)
- the patient's comorbid psychiatric or medical conditions
- clinician familiarity with specific antidepressants

In order to get Food and Drug Administration (FDA) approval as a generic bioequivalent, the compound must be 80% to 125% bioequivalent to the brand product. There is no evidence regarding choice of brand versus generic based on adverse clinical outcomes.

Consider discussing with the patient the specific side effect profiles, costs, and benefits of different antidepressants, including generics.

1. Selective Serotonin Reuptake Inhibitor (SSRI): venlafaxine; mirtazepine; and bupropion

   SSRIs, venlafaxine, mirtazepine and bupropion are frequently chosen as first-line therapy because of simplicity, side effect profiles and community standards.

   They generally lack the common adverse reactions (anticholinergic, sedative effects) of the tricyclics and cause fewer problems when

taken in overdose. However, they may cause headache, nervousness, insomnia, and sexual side effects and may be more expensive as many may not yet be available as generics. Care must be taken to remain with either the brand name product or the same general product. Do not switch from brand to generic or between generics.

2. Secondary Amine Tricyclics

   The literature clearly supports the effectiveness of tricyclics. Because of associated side effects, they are used less frequently as first-line agents. Secondary amine tricyclics cause less orthostatic hypotension and sedation than tertiary amine tricyclics.

3. Monoamine Oxidase Inhibitor (MAOI)

   MAOIs, in general, should be restricted for patients who do not respond to other treatments because of their potential for serious side effects and the necessity of dietary restrictions. Patients with major depressive disorders with atypical features are one group for whom several studies suggest MAOIs may be particularly effective. However, in clinical practice, many psychiatrists start with SSRIs in such patients because of the more favorable adverse effect profile.

Medication interactions with antidepressant agents: Many antidepressant agents have clinically significant drug interactions, particularly those agents which undergo cytochrome P450 enzymatic metabolism in the liver. A complete discussion of this topic is beyond the scope of this guideline. Practitioners are advised to consult references such as The Physician's Desk Reference, American Hospital Formulary Service, Epocrates, or Micromedex for more information about drug interactions with specific agents, and to assess the significance of the interaction prior to prescribing antidepressants.

Evidence supporting this recommendation is of class: R

Elderly patients: Because of the potential for decreased renal and hepatic function, concomitant diseases, and medications, the elderly are at higher risk of significant side effects or drug interactions with antidepressant medications. Consider starting at the lowest possible dose and increasing slowly to effective dose or until side effects appear. Tertiary amine tricyclics should generally be avoided in elderly patients because of the high incidence of orthostatic hypotension, sedation, and cardiac effects with these agents.

Evidence supporting this recommendation is of classes: A, C

Pregnancy: Approximately 5 to 10% of women experience significant mood or anxiety symptoms during pregnancy. Physicians must help patients weigh the risk of prenatal exposure to psychotropic medications against the risks of untreated psychiatric illness. The first line of treatment for mild to moderate depression includes increased social supports and psychotherapy. When these non-medication options have failed or if patients have severe major depression or other Axis I diagnoses, then the risks of untreated illness may

outweigh the potential detrimental effects of certain psychotropic medications.

Patients commonly under estimate the risks of untreated maternal psychiatric illness while over emphasizing the risks of their psychotropic medications. Misperception about risk can lead both physicians and patients to terminate otherwise wanted pregnancies or avoid needed pharmacotherapy. By informing patients about the nature and magnitude of medication risks as well the risks of untreated illness, psychiatrists can help patients reach their own decisions.

US Food and Drug Administration (FDA) Pregnancy Risk Categories: (A) Controlled studies show no risk. Adequate, well-controlled studies in pregnant women have failed to demonstrate risk to the fetus. No currently available antidepressant medication is rated A. (B) No evidence of risk in humans. Either animal findings show risk, but human findings do not; or if no adequate human studies have been done, animal findings are negative. Bupropion and maprotiline are rated B. (C) Risk cannot be ruled out. Human studies are lacking, and animal studies are either positive for fetal risk or lacking. However, potential benefits may justify the potential risks. Amitriptyline, amoxapine, protriptyline, sertraline, trazodone, trimipramine, venlafaxine are rated C. (D) Positive evidence of risk. Investigational or post-marketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risks. If needed in a life-threatening situation or a serious disease, the drug may be acceptable if safer drugs cannot be used or are ineffective. Imipramine and nortriptyline are rated D. (X) Contraindicated in pregnancy. Studies in animals or human, or investigational or postmarketing reports have shown fetal risk which clearly outweighs any possible benefit to the patient. None of the currently available antidepressant medications are rated X.

Among antidepressants, the most reproductive safety information is available for the tricyclic antidepressants (TCAs), fluoxetine, and citalopram. Among the available pregnancy data, there is no evidence that these medications are associated with an increased risk of major congenital malformations. This is also true for sertraline, paroxetine, fluvoxamine, venlafaxine, and bupropion; however, there are fewer documented pregnancies with these medications.

There have been many case reports of perinatal syndromes with TCAs (e.g., jitteriness, irritability, bowel obstruction, urinary retention) as well as different SSRIs (e.g., fluoxetine, paroxetine, and sertraline). Other studies have found an association between prenatal SSRI exposure and preterm delivery. In general, however, these reports have been limited to case reports and small series. To avoid perinatal withdrawal syndromes, some support slowly tapering antidepressants in the weeks prior to delivery. This is a debated treatment strategy since it also theoretically withdraws antidepressants just as women are entering the postpartum period, a time of increased risk for mood or anxiety symptoms.

Evidence supporting this recommendation is of classes: B, C, R

Lactation: Antidepressants may appear in breast milk in low concentrations. Because of the long half-life of these drugs and their metabolites, nursing

infants may have measurable amounts in their plasma and tissues, such as the brain. This is particularly important during the first few months of life, with immature hepatic and renal function. Because these drugs affect neurotransmitter function in the developing central nervous system, it may not be possible to predict long-term neurodevelopmental effects. Use only when clearly needed and potential benefits outweigh the risks to the nursing infant. (Adapted from American Academy of Pediatrics [AAP] Policy Statement, Transfer of Drugs and Other Chemicals Into Human Milk, Pediatrics 2001;108:776-789). Breast-feeding offers several advantages: a) Breast-fed infants have lower rates of gastrointestinal disease, anemia, respiratory ailments, and otitis media compared to formula-fed infants; b) Nursing provides a unique opportunity for maternal-infant bonding. At the same time, the postpartum period (first 3 months following childbirth) is a particularly vulnerable period for psychiatric illness in women. Issues to be addressed when assessing the risks and benefits of psychotropic drug use during breast-feeding include the documented benefits of nursing, the potential adverse impact of untreated maternal mental illness on infant attachment and cognitive and behavioral development, and the effects of untreated mental illness on the mother.

Depression in the postpartum period can be disabling. Trials of cognitive behavioral therapy or interpersonal therapy, while safe, may not be effective – resulting in the need for antidepressant trials and/or electroconvulsive therapy (ECT). The use of antidepressants by nursing mothers is often acceptable as long as the mother-infant pair is monitored for the emergence of adverse effects or complications. Tricyclic antidepressants appear to be safe. However, there was one case report of respiratory distress in an infant of a mother treated with doxepin suggesting that this antidepressant should be avoided during lactation. Data on the SSRIs suggest that sertraline and paroxetine are safe to use in nursing mothers suffering from depression. The data on fluoxetine is more difficult to interpret. The few adverse effects that have been reported in the literature have been transient and not verified by medical personnel. The lack of adverse effects in 180 exposed infants to fluoxetine justifies its use especially if prescribed during the pregnancy or if there is a preferential history of response to this medication. Data on citalopram, fluvoxamine, bupropion and venlafaxine are more limited and their use cannot be recommended during breast-feeding at this time.

Evidence supporting this recommendation is of classes: C, R

Refer to the original guideline document for dosage recommendations.

For further prescribing information the following drug references may be used:

- The Physicians Desk Reference
- The American Hospital Formulary Service (AHFS)
- Micromedex
- Epocrates

Evidence supporting this recommendation is of class: R

Herbals and Dietary Supplements

Caution: many drugs interact with St. John's wort, including other antidepressants, warfarin, oral contraceptives, antiretroviral, anti-cancer and anti-rejection drugs. Care should be taken to ask all patients what medications they are taking, including over-the-counter and supplements, to avoid these interactions.

Hypericum perforatum (St. John's wort) is popularly thought to be an herbal remedy for depression. The Hypericum Depression Trial Study Group concluded that the data does not support the use of Hypericum perforatum instead of antidepressants or psychotherapy. It has no proven efficacy in standard clinical care of patients with major depression.

SAM-e (S-adenosyl methionine) S-Adenosyl - L-methionine (SAM-e) is a natural compound that has been studied as a treatment option for depression. As of 2002, there were 11 controlled against placebo studies, 14 controlled against tricyclic antidepressant studies, and 2 meta-analyses. Essentially these studies show that SAM-e is superior to placebo and comparable to tricyclics in the treatment of outpatients with major depression. Effective oral doses seem to be in the 400-1,600 mg a day range as compared to doses of 400 mg a day of tricyclics. Side effects are less common than with tricyclics (7% with oral and intramuscular SAM-e versus 28% with oral tricyclic) and include mild insomnia, lack of appetite, constipation, nausea, dry mouth, diaphoresis, dizziness and nervousness. Increased anxiety and hypomania have been reported in patients with bipolar depression. Interactions with other medications have not been studied and are unknown. Comparisons to newer antidepressants have not been done yet.

Other herbal remedies and dietary supplements, such as kava-kava, Omega-3 fatty acid, (docosahexaenoic acid) and valerian root, have not been proven effective for the treatment of depression and may or may not be safe.

Herbal products and nutritional supplements are not evaluated or regulated by the U.S. Food and Drug Administration for safety, efficacy or bioavailability.

Evidence supporting this recommendation is of classes: A, M, R

Establish Follow-Up Plan

Establish and maintain initial follow-up contact intervals (office, phone, other).

Improving attitudes towards antidepressant medications along with the patient's ability to handle medication side effects are key factors in promoting greater adherence to maintenance treatment and thus greater likelihood of preventing relapse. Interventions toward this end may include patient visits with a depression prevention specialist (PhD, MSN, MSW who has received special training) and follow-up phone calls. Interventions are critical to

educating the patient regarding the importance of preventing relapse, safety and efficacy of medications and management of potential side effects.

If symptoms are severe, weekly contacts are appropriate. Contact should be every 2-4 weeks if mild or moderate symptoms are present. This protocol should be in place until remission or best possible response is achieved, then treatment should be spaced out as clinically warranted.

Office visits for maintenance medication can occur every 3-12 months if everything else is stable.

Referral

Consider involvement of a behavioral health care provider for the following:

- Patient request for psychotherapy
- Presence of severe symptoms and impairment in patient
- Diagnostic question
- Presence of other psychiatric condition (e.g., personality disorder, history of mania)
- Substance abuse questions
- Clinician discomfort with the case
- Initial treatment does not result in a successful outcome
- Patient request for more specialized treatment

Evidence supporting this recommendation is of classes: A, M, R

11. Is Patient Responding Adequately?

The goal is to achieve a significant reduction of symptoms. Assessment includes evaluation of symptoms, work or school attendance and productivity, and quality of interpersonal interactions. There is no professional consensus on what represents an adequate antidepressant trial or patient response. Two of the most common causes of inadequate response are: (1) insufficient dosage; and (2) inadequate duration of treatment.

A patient's response to antidepressant treatment should be evaluated between 4 and 6 weeks. A reasonable criterion for extending the initial treatment is if the patient is experiencing a 25% or grater reduction in baseline symptom severity. If the patient's symptoms are reduced by 25% or more, but they are not yet at remission, and if medication has been well tolerated then continue to prescribe and raising the dose as recommended. Improvement with psychotherapy is often a bit slower than with pharmacotherapy. A decision regarding progress with psychotherapy and the need to change or augment this type of treatment may require 8 to 10 weeks before evaluation.

Evidence supporting this recommendation is of classes: A, M

12. Evaluate Dose, Duration, Adherence with Medication and/or Psychotherapy/Reconsider Accuracy of Diagnosis, or Impact of Comorbidities

When patients do not respond to initial antidepressant treatment, clinicians should take the following steps:

1. Reevaluate the diagnosis
2. Evaluate comorbid diagnoses

   Substance abuse and personality disorders are often overlooked and confounding. Reevaluate for the presence of medical conditions.

3. Medication Adherence

   Useful strategies are to review adherence to the medication regimen with the patient and family and check with the pharmacy about frequency of refills.

4. Evaluate dose

   If side effects are tolerable, increase the antidepressant dose. Serum levels of four tricyclic antidepressants are sometimes useful. For nortriptyline, a curvilinear plasma level/therapeutic response relationship exists between 50 and 150 ng/ml. For desipramine, the relationship between serum level and response is linear, with the threshold for therapeutic response being 116 ng/ml (sensitivity 81%, specificity 59%). For imipramine, a linear relationship exists between antidepressant response and serum levels of desipramine plus imipramine of 175 to 350 ng/ml. The data for amitriptyline are weakest and indicate a linear relationship at serum levels of amitriptyline plus nortriptyline of 93 to 140 ng/ml (sensitivity 37%; specificity 80%).

   Other than for the four agents noted above, serum levels are rarely useful for antidepressants, including SSRIs, bupropion, nefazodone, venlafaxine, mirtazapine, and other tricyclics, unless one is checking for compliance.

5. Consider a longer medication trial

   Duration

   Although there is limited scientific data to guide the clinician, an adequate trial of an antidepressant is usually considered to be 4 to 6 weeks. However, duration should not be assessed until the dose is well within the usual therapeutic range. Once that occurs, consider other strategies (see Annotation #14, "Continuation and Maintenance Treatment for 6-12 Months") if there is no response or a minimal response after 4 to 6 weeks.

6. Consider consultation with colleagues

Evidence supporting this recommendation is of classes: A, R

13. Consider Other Strategies

Switch Therapy

If the patient has been treated with a medication and there is less than 25% reduction in symptoms when evaluated at 4 to 6 weeks, switch to a different medication. If there is a partial response and side effects are not prohibiting, increase the dose. As part of the evaluation, using a standardized assessment tool will serve as a documentation of progress.

If the above measures have not achieved remission when reevaluated 4 to 6 weeks later, consider:

- Switching to a different medication; augmentation strategies (such as lithium or low-dose thyroid); other biological treatments (such as a second antidepressant); adding a new medication
- Referral to psychiatry for possible MAOI, treatment for electroconvulsive treatment (ECT)
- Looking for comorbidities, such as substance abuse issues
- Referrals, if there are personality disorders and/or substance abuse issues present
- If only on medication, add psychotherapy
- Whether adequate engagement of patient/family is present and that recommendations are being followed (adherence)
- Obtaining a consultation or referral to other behavioral health specialists
- Reevaluating the diagnosis

Evidence supporting this recommendation is of classes: A, B, D

Augmentation Therapies

Augmentation therapy is used for those situations where the patient's depression is either treatment resistant or only partially responsive to treatment. This is a good time to consult and/or refer to an additional behavioral health care specialist.

Augmentation therapies include:

1. Lithium augmentation with tricyclic antidepressants (TCAs).
2. Lithium augmentation with SSRI (caution - serotonin syndrome).
3. Triiodothyronine (T_3) augmentation of TCA.
4. Stimulant drugs augmentation of TCA/SSRI ("jump-start response").
5. TCA-SSRI combination (caution - elevated TCA level - to be monitored).
6. Bupropion - SSRI combination.
7. Mirtazapine - SSRI combination.

8. Buspirone - SSRI combination.
9. Carbamazepine/valproic acid - TCA combination (caution - may decrease TCA level).
10. Carbamazepine/valproic acid - SSRI combination.
11. Low dose risperidone - SSRI combination.

Evidence supporting this recommendation is of classes: A, C, D, R

Other Biological Therapies

Electroconvulsive treatment (ECT) is very effective and can sometimes be administered safely in an outpatient setting. Factors that may suggest an increased response to electroconvulsive treatment:

1. Geriatric depression
2. Antidepressant medications have not been tolerated or pose a significant medical risk.
3. Antidepressant medication trials have not been successful.
4. ECT has been successful in previous episodes.
5. Catatonia is present.
6. A rapid response is needed because of severe suicide risk or because the patient's health has been significantly compromised by the depression (i.e., severe cachexia, inability to attend to the activities of everyday living).
7. Depression with psychotic features.
8. Melancholic symptoms are predominant.
9. Depression and parkinsonism.

The literature supports a dose response effect from ECT, with higher doses per treatment leading to improved outcomes.

Evidence supporting this recommendation is of classes: A, B, M, R

Vagus Nerve Stimulation

Vagus nerve stimulation (VNS) generally refers to stimulation of the left vagus nerve at the cervical level. It requires surgical implementation and in psychiatry has generally been studied in treatment resistant nonpsychotic depression. VNS most common side effects included voice alteration (hoarseness), dyspnea and neck pain.

Although a number of non-blinded studies have shown reasonable response/remission rates in treatment resistant depression, the single placebo controlled randomized trial failed to corroborate this. Currently this treatment cannot be considered evidence based.

Evidence supporting this recommendation is of classes: D, R

Transcranial Magnetic Stimulation

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique that stimulates the brain in vivo using high intensity, pulsed electron-magnetic fields. Recent research has examined the use of rTMS in the treatment of major depressive disorder. In the procedure, a hand-held stimulating coil is applied directly to the patient's head and delivers a magnetic pulse to the cortex. Results of research studies to date have been inconsistent and inconclusive. There is not adequate data at this time to support the use of rTMS in treating depression.

Evidence supporting this recommendation is of classes: C, M

Light Therapy

Use of bright light therapy for treatment of major depression with a seasonal specifier is well established. Additionally, there is preliminary evidence of the efficacy of bright light therapy for some other types of depressive symptom patterns, including non-seasonal depression and milder variations of seasonal depressive patterns. Bright light therapy may also quicken and enhance the effects of antidepressant medication. A recent open study of light therapy for treatment of major depression during pregnancy yielded promising results, although further research is needed to clearly establish safety and efficacy during pregnancy. Although the light exposure dosage (typically 5,000-10,000 lux) and exposure length (typically 30-60 minutes) have been fairly standard for seasonal affective disorder treatment, research on bright light therapy for other types of depression has not necessarily utilized standard dosages and exposure times. It is important that any light therapy treatment utilize equipment that eliminates ultraviolet frequencies and produces bright light of known spectrum and intensity. For these reasons, use of client-constructed light therapy units is contraindicated.

Evidence supporting this recommendation is of classes: A, D, M, R

Acupuncture

Although acupuncture is known to be an alternative therapy for the treatment of depression, it has shown mixed results. Acupuncture may be an alternative for those who reject traditional treatments, for those who do not show adequate response to traditional treatments or for those in whom antidepressants may be contraindicated (frail, elderly or pregnant women). Electro-acupuncture may be a treatment of choice for those who are unable to comply with classic tricyclic antidepressants because of their anticholinergic side effects. It is felt that additional larger and controlled studies need to be done before this can be endorsed as a recommended treatment for depression.

Evidence supporting this recommendation is of classes: A, R

Psychotherapies

If patient is newly involved in psychotherapy

- Return visit in 8-10 weeks to evaluate progress
- Contact with patient in 4-6 weeks
- Communicate with therapist in 4-6 weeks
- Therapy can take 8-10 weeks to show improvement

Randomized, controlled studies of the efficacy of psychotherapy in the treatment of depression are few. Moreover, comprehensive reviews of these studies support the superiority of time-limited, content- and procedure-specific therapies such as cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT). There is fewer but recent data that support the efficacy of problem-solving therapy (PST) and brief psychodynamic supportive psychotherapy (PSP) in treating depression. PSP in combination with pharmacotherapy has been found to be more effective than pharmacotherapy alone for depressed patients with comorbid personality disorders. PST or PSP should be considered if CBT or IPT is not available or as a second-line psychotherapy treatment. There are fewer studies, but it appears that with mild and moderate levels of major depression, CBT, IPT and antidepressant medications are equally effective. With severe depression, antidepressant medication may be more helpful in the acute phases. Relapse rates are lower with therapy than with medication treatment.

Hospitalization

Partial or full hospitalization may be indicated in patients who have failed outpatient management.

14. Continuation and Maintenance Treatment for 6 to 12 Months

Major depression is now recognized as a recurrent, sometimes chronic, long-term illness. Treatment of major depressive disorder is divided into acute, continuation, and maintenance phases.

Acute treatment (usually the first 3 months) refers to use of antidepressant medication to strive for remission of major depressive symptoms. Remission is defined as having minimal residual symptoms (Hamilton Depression Scale score less than 7 or PHQ-9 score of 4 or less). Continuation therapy is the phase where one continues to treat with antidepressants in order to keep the patient free of symptoms for the duration of the current episode. By definition, this is considered to be at least 6 months long, but lately more authors are viewing the duration as 6 to 12 months long. However, consider in elderly populations it may take longer to respond to acute treatment. Therefore, the maintenance period may need to be extended. Maintenance therapy is designed to prevent recurrence of new or future episodes of depression. Please see Discussion and References #14 in the original guideline document for references to recent evidence-based literature that suggests treating more types of depressed patients with adequate dosages of antidepressants for longer periods is more effective in preventing relapses and reoccurrence. An adequate dose is generally considered to be the same as the dose required in the acute phase of treatment in order to achieve remission.

Recommended Guidelines for Treatment of Depression (Treatment Duration)

First episode: 6 - 12 months
Second episode: 3 years
Second episode with complicating factors (previous dysthymia): Lifetime
Third episode: Lifetime

Complicating factors are those situations where evidence either shows or suggests higher rates of recurrence after stopping antidepressants and include:

- Preexisting dysthymia
- Pattern of increasing frequency of episodes
- Inability to achieve remission
- Recurrence of symptoms in response to previously attempted discontinuation

With the wide array of half-lives and therapeutic dose ranges for the various existing antidepressants, it is beyond the scope of this guideline to discuss detailed discontinuation strategies.

When feasible (e.g., the starting dose is not the same as therapeutic doses), it is recommended that the dose be tapered over a period of weeks to several months when discontinuing an antidepressant.

Definitions:

Classes of Research Reports:

A. Primary Reports of New Data Collection

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study

- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

A detailed and annotated clinical algorithm is provided for Major Depression In Adults For Mental Health Care.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline contains an annotated bibliography and discussion of the evidence supporting each recommendation. The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Increased use of Diagnostic and Statistical Manual of Mental Disorders, 4th edition Text Revision (DSM-IV TR) criteria in the detection and diagnosis of major depression
- Improved efficacy of the treatment through diagnosis of depression
- Improved outcomes of treatment for major depression
- Improved adherence and maintenance of appropriate treatments by having follow-up contacts with a health care professional
- Improved communication between the primary care physician and the mental health care provider (if patient is comanaged)
- Reduction and remission of symptoms of depression
- Reduction of recurrence of major depression

POTENTIAL HARMS

Side Effects of Anti-depressant Medication

- Selective serotonin re-uptake inhibitors (SSRIs), venlafaxine, mirtazepine and bupropion may cause headache, nervousness, insomnia, and sexual side effects and may be more expensive as most are not yet available as generics. Care must be taken to remain with either brand name product or the same generic product. Do not switch from brand to generic or between generics.
- Secondary amine tricyclics are used less frequently as first-line therapy because of associated side effects.
- Monoamine oxidase inhibitors (MAOIs) should be restricted for patients who do not respond to other treatments because of their potential for serious side effects and the necessity of dietary restrictions.
- Lithium augmentation with selective serotonin reuptake inhibitors poses the risk of serotonin syndrome due to elevation of serum levels of the tricyclics.
- Many antidepressant agents have clinically significant drug interactions, particularly those agents which undergo cytochrome P450 enzymatic metabolism in the liver.

Subgroups Most Likely to Be Harmed

- Elderly patients: Because of the potential for decreased renal and hepatic function, concomitant diseases and medications, the elderly are at higher risk of significant side effects or drug interactions with antidepressant medications. Tertiary amine tricyclics should generally be avoided in elderly patients because of the high incidence of orthostatic hypotension, sedation, and cardiac effects with these agents.
- Pregnant Women: There have been many case reports of perinatal syndromes with TCAs (e.g., jitteriness, irritability, bowel obstruction, urinary retention) as well as different SSRIs (e.g., fluoxetine, paroxetine, and sertraline). Other studies have found an association between prenatal SSRI exposure and preterm delivery. In general, however, these reports have been limited to case reports and small series.
- Antidepressants may appear in breast milk in low concentrations. Because of the long half-life of these drugs and their metabolites, nursing infants may have measurable amounts in their plasma and tissues, such as the brain. This is particularly important during the first few months of life, with immature hepatic and renal function. Because these drugs affect neurotransmitter function in the developing central nervous system, it may not be possible to predict long-term neurodevelopmental effects. Use only when clearly needed and potential benefits outweigh the risks to the nursing infant.

CONTRAINDICATIONS

CONTRAINDICATIONS

Use of client-constructed light therapy units is contraindicated.

QUALIFYING STATEMENTS

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- This clinical guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

RELATED NQMC MEASURES

- Major depression in adults for mental health care: percentage of patients with a new diagnosis of major depression, with documentation of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV TR) criteria within the three months prior to initial diagnosis.
- Major depression in adults for mental health care: percentage of patients whose results on 2 quantitative symptom assessment tools (such as Patient Health Questionnaire [PHQ-9]) decrease by 50 percent within six months of initiating treatment.
- Major depression in adults for mental health care: percentage of patients whose results on 2 Patient Health Questionnaires (PHQ-9s) score less than 5

or similar testing (Hamilton Depression Scale 7 or less) within 6 months of initiating treatment.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Major depression in adults for mental health care. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 May. 52 p. [154 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT SpecialtyCare, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, Hamm Clinic, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hennepin Faculty Associates, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Health Care, North Suburban Family Physicians,

NorthPoint Health &: Wellness Center, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, St. Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Winona Health

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GUIDELINE COMMITTEE

Committee on Evidence-Based Medicine

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform

users. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

No work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Major depression in adults for mental health care providers. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Sep. 49 p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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